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10/066,443	02/05/2002	Bruce Spiegelman	DFN-038	3678

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	6

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	10/066,443	SPIEGELMAN ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-77 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-77 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Claims 1-77 are pending.

It is noted that the amino acid sequence (LXXLL) has a SEQ ID NO in the sequence listing. However, the amino acid sequence in the specification and claims does not have the corresponding SEQ ID NO:. The application does not comply with § 1.821 (d). To comply with § 1.821 (d) and to forestall objections in an action on the merits, it is suggested that applicants amend the amino acid sequence in the specification and claims with the corresponding SEQ ID NO: (SEQ ID NO: 3) in their response to the restriction.

Claim 9 does not further limit claim 7 or 8 because the nucleic acid sequence in claim 8 does not comprise the nucleic acid in claim 9, wherein nucleotides 518-532 of SEQ ID NO: 4 are deleted. Claim 9 will be read as if it depends from claim 6.

Claim 21 does not further limit claim 19 or 20 because the PGC-1 polypeptide in claim 20 does not comprise the polypeptide in claim 21, wherein residues 144-148 of SEQ ID NO: 5 are deleted. Claim 21 will be read as if it depends from claim 18.

Claim 66 does not further limit claim 64 or 65 because the nucleic acid sequence in claim 65 does not comprise the nucleic acid in claim 66, wherein nucleotides 518-532 of SEQ ID NO: 4 are deleted. Claim 66 will be read as if it depends from claim 63.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 7 and 8, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with a nucleic acid encoding PGC-1, classifiable in class 435, subclass 375.

II. Claims 9-14, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 expression, wherein the agent is a PGC-1 nucleic acid encodes a dominant negative PGC-1 polypeptide, classifiable in class 435, subclass 375.

III. Claim 15, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 expression, wherein the agent is a PGC-1 nucleic acid is an antisense PGC-1 nucleic acid molecule, classifiable in class 435, subclass 375.

IV. Claim 19 and 20, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that increases PGC-1 activity, wherein the agent is a PGC-1 polypeptide, classifiable in class 435, subclass 375.

V. Claim 21-26, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 activity, wherein the agent is a dominant negative PGC-1 polypeptide, classifiable in class 435, subclass 375.

VI. Claim 27, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that **increases** PGC-1 expression,

wherein the agent is a polypeptide that binds PGC-1, classifiable in class 435, subclass 375.

VII. Claim 27, drawn to an in vitro method for modulating gluconeogenesis comprising contacting a cell with an agent that **decreases** PGC-1 expression, wherein the agent is a polypeptide that binds PGC-1, classifiable in class 435, subclass 375.

VIII. Claims 7, 8, and 64-65, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that increases PGC-1 expression, wherein the agent is a nucleic acid encoding PGC-1, classifiable in class 424, subclass 93.2.

IX. Claims 9-14, 66, and 68-72, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 expression, wherein the agent is a PGC-1 nucleic acid encodes a dominant negative PGC-1 polypeptide, classifiable in class 424, subclass 93.2.

X. Claim 15 and 67, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 activity, wherein the agent is a PGC-1 nucleic acid is an antisense PGC-1 nucleic acid molecule, classifiable in class 514, subclass 44.

XI. Claims 19 and 20, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that increases PGC-1 activity, wherein the agent is a PGC-1 polypeptide, classifiable in class 514, subclass 2.

XII. Claims 21-26, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that decreases PGC-1 activity, wherein the agent is a dominant negative PGC-1 polypeptide, classifiable in class 514, subclass 2.

XIII. Claim 27, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that **increases** PGC-1 expression, wherein the agent is a polypeptide that binds PGC-1, classifiable in class 424, subclass 139.1.

XIV. Claim 27, drawn to an in vivo method for modulating gluconeogenesis comprising contacting a cell with an agent that **decreases** PGC-1 expression, wherein the agent is a polypeptide that binds PGC-1, classifiable in class 424, subclass 139.1.

XV. Claim 37, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein PGC-1 expression is directly measured by Northern blotting, classifiable in class 435, subclass 6.

XVI. Claim 39, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein determining whether PGC-1 activity is modulated comprises determining

expression level of PEP-CK, wherein PEP-CK expression is measured by Northern blotting, classifiable in class 435, subclass 6.

XVII. Claim 39, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein determining whether PGC-1 activity is modulated comprises determining expression level of glucose-6-phosphatase, wherein expression of glucose-6-phosphtase is measured by Northern blotting, classifiable in class 435, subclass 6.

XVIII. Claim 39, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein determining whether PGC-1 activity is modulated comprises determining expression level of fructose-1,6-bisphosphatase, wherein expression of fructose-1,6-bisphohpatase is measured by Northern blotting, classifiable in class 435, subclass 6.

XIX. Claim 40, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein expression is measure by measuring the expression or activity of a reporter construct comprising the promoter/enhancer region from phosphoenolpyruvate carboxykinase, classifiable in class 435, subclass 29.

XX. Claim 40, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein expression is measure by measuring the expression or activity of a reporter construct comprising the promoter/enhancer region from glucose-6-phophatase, classifiable in class 435, subclass 29.

XXI. Claim 40, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated, wherein expression is measure by measuring the expression or activity of a reporter construct comprising the promoter/enhancer region from fructose-1,6-bisphosphatase gene, classifiable in class 435, subclass 29.

XXII. Claim 41, drawn to a method for identifying a compound capable of modulating gluconeogenesis comprising: a) contacting a cell with a compound; and b) determining whether PGC-1 expression or activity is modulated comprises determining whether glucose output from the cell is modulated, classifiable in class 435, subclass 4.

XXIII. Claim 51, drawn to a method for identifying a compound which inhibits the interaction of the PGC-1 protein with a target molecule comprising contacting, in the presence of the compound, the PGC-1 protein and the target molecule under conditions which allow binding of the target molecule to the PGC-1 protein to

form a complex, wherein the target molecule is HNF-4alpha, classifiable in class 435, subclass 7.1.

XXIV. Claim 52, drawn to a method for identifying a compound which inhibits the interaction of the PGC-1 protein with a target molecule comprising contacting, in the presence of the compound, the PGC-1 protein and the target molecule under conditions which allow binding of the target molecule to the PGC-1 protein to form a complex, wherein the target molecule is phosphoenolpyruvate carboxykinase promoter, classifiable in class 435, subclass 7.1.

XXV. Claims 75-77, a compound with an unspecified structure identified by the method of claim 34, 44, or 50, unclassifiable because the claims do not provide a structural description of the compound.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-VII and Inventions VIII-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The in vitro methods in inventions I-VII are directed to distinct methods that have different modes of operation, different function and different effect than the in vivo methods in inventions VIII-XIV. Administering an agent to an in vitro cell would have different effect, different function, and different mode of operation than administering an agent to a whole organism. The specification does not disclose that the methods are disclosed as capable of use together.

Furthermore, the nucleic acid encoding PGC-1 in Invention I and invention VIII have a different function and different effect than the nucleic acid encoding a PGC-1 dominant negative

polypeptide in Invention II and IX; the antisense PGC-1 nucleic acid molecule in invention III and X; the polypeptide in invention IV and XI, the dominant negative PGC-1 polypeptide invention V and XII; and the polypeptide that binds PGC-1 in inventions VI, VII, XIV and XV. Inventions I, IV, VI, VIII, XI, and XIII are directed to increasing PGC-1 activity or expression and Inventions II, III, V, VII, IX, X, XII, and XIV are directed to decreasing PGC-1 activity or expression.

In addition, the different classification of each invention further displays that it would be an undue burden on the examiner to search the entire claimed invention because each group requires a different search.

Inventions I-XIV and Inventions XV-XXIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed distinct methods that have different modes of operation, different function and different effect. Inventions I-XIV are directed to modulating gluconeogenesis in either an in vitro or a subject and Inventions XV-XXIV are directed to identifying a compound capable of modulating gluconeogenesis. The specification does not disclose that the methods are disclosed as capable of use together.

Inventions XV-XXIV have a different mode of operation and different function. Invention XV is directed to measuring PGC-1 expression using Northern blotting and Inventions XVI-XVIII are directed to measuring PEPCK, glucose-6-phosphotase, or fructose-1,6-bisphosphatase expression using Northern blotting. Inventions XIX-XXI are directed to a

reporter assay using a promoter/enhancer region from PEPCK, glucose-6-phosphotase, or fructose-1,6-bisphosphatase operatively linked to a reporter gene.

In addition, the different classification of each invention further displays that it would be an undue burden on the examiner to search the entire claimed invention because each group requires a different search.

Invention XXV and Inventions I-XXIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the test compound in invention XXV can be identified by any method in Groups listed above and can be a compound (e.g. polynucleotide sequence, organic compound, peptide, polypeptide, antibody) and these compounds are distinct compounds with distinct structures and functions and could be used in a therapeutic method for genetic diseases, wherein said method comprises modulating gluconeogenesis. The methods in inventions XIV-XXIII also used products that do no have any effect and that are not readable on the product in invention XXV. In addition, the different classification of each invention further displays that it would be an undue burden on the examiner to search the entire claimed invention because each group requires a different search.

Claims 1, 28, 30, and 31 link(s) inventions I-XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1, 28, 30, and

31. With respect to claim 31 reciting a Fao hepatoma cell, the hepatoma cell line only links inventions I-VII because this is a cell line only found in vitro.

Claims 2 and 4 link(s) invention I, IV, VI, VIII, XI, and XIII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 2 and 4.

Claims 3 and 5 link(s) invention II, III, V, VII, IX, X, XII, and XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 3 and 5.

Claim 6 link(s) invention I, II, III, and VIII-X. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 6.

Claim 16, 17, 73 and 74 link(s) invention I, II, VIII, and IX. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 16, 17, 73, and 74.

Claim 18 link(s) invention IV, V, XI, and XII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 18.

Claim 29 link(s) invention II, III, V, VII, IX, X, XII, and XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 29.

Claim 32 link(s) invention I-VII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 32.

Claim 33 link(s) invention VIII-XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 33.

Claims 34-36 link(s) invention XV-XXII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 34-36.

Claim 38 link(s) invention XVI-XXI. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 38.

Claims 42-49 link(s) invention XV-XXII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 42-49.

Claim 50 link(s) invention XXIII and invention XXIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 50.

Claim 53 link(s) inventions VIII-XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 53.

Claims 54-57, 59, and 61 link(s) invention IX, X, XII, and XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 54-57, 59, and 61.

Claims 58, 60, and 62 link(s) invention VIII, XI, and XIII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 58, 60, and 62.

Claim 63 link(s) invention VIII, IX, and X. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 63.

Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all

the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Because these inventions are distinct for the reasons given above and the search required for each Group set forth above is not required for any other Group listed above and the search for each group is not co-extensive, restriction for examination purposes as indicated is proper.

It would be unduly burdensome for the examiner to search and consider patentability of all of the presently pending claims, a restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER